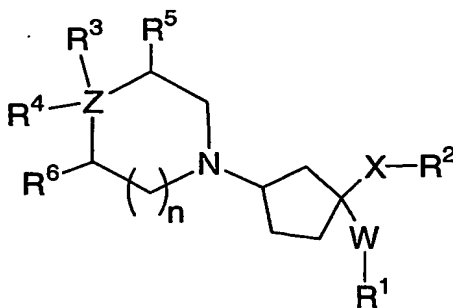


## WHAT IS CLAIMED IS:

1. A compound of the formula I:



I

wherein:

X is selected from the group consisting of:

-NR<sup>10</sup>-, -O-, -CH<sub>2</sub>O-, -CONR<sup>10</sup>-, -NR<sup>10</sup>CO-, -CO<sub>2</sub>-, -OCO-,  
-CH<sub>2</sub>(NR<sup>10</sup>)CO-, -N(COR<sup>10</sup>)-, -CH<sub>2</sub>N(COR<sup>10</sup>)-, phenyl, and  
C<sub>3</sub>-6 cycloalkyl,

where R<sup>10</sup> is independently selected from: hydrogen, C<sub>1</sub>-6 alkyl, benzyl,  
phenyl, and C<sub>1</sub>-6 alkyl-C<sub>3</sub>-6 cycloalkyl,

which is unsubstituted or substituted with 1-3 substituents where the  
substituents are independently selected from: halo, C<sub>1</sub>-3 alkyl,  
C<sub>1</sub>-3alkoxy and trifluoromethyl;

W is selected from:

phenyl and heterocycle, which is unsubstituted or substituted with 1-3  
substituents where the substituents are independently selected from:  
halo, C<sub>1</sub>-3alkoxy and trifluoromethyl;

Z is selected from:

C, N, and -O-, wherein when Z is N, then R<sup>4</sup> is absent, and when W is -O-,  
then both R<sup>3</sup> and R<sup>4</sup> are absent;

n is an integer selected from 0, 1, 2, 3 and 4;

R<sup>1</sup> is selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- 5 (d) hydroxy,
- (e) C<sub>1</sub>-6alkyl,
- (f) C<sub>3</sub>-7cycloalkyl,
- (g) -O-C<sub>1</sub>-6alkyl,
- (h) -O-C<sub>3</sub>-7cycloalkyl,
- 10 (i) -SCF<sub>3</sub>,
- (j) -S-C<sub>1</sub>-6alkyl,
- (k) -SO<sub>2</sub>-C<sub>1</sub>-6alkyl,
- (l) phenyl,
- (m) heterocycle,
- 15 (n) -CO<sub>2</sub>R<sup>9</sup>,
- (o) -CN,
- (p) -NR<sup>9</sup>R<sup>10</sup>,
- (q) -NR<sup>9</sup>-SO<sub>2</sub>-R<sup>10</sup>,
- (r) -SO<sub>2</sub>-NR<sup>9</sup>R<sup>10</sup>, and
- 20 (s) -CONR<sup>9</sup>R<sup>10</sup>
- (t) -NHC(=NH)NH<sub>2</sub>, and
- (u) hydrogen,

R<sup>2</sup> is selected from:

- 25 (C<sub>0</sub>-6alkyl)-phenyl and (C<sub>0</sub>-6alkyl)-heterocycle,
- where the alkyl is unsubstituted or substituted with 1-7 substituents
- where the substituents are independently selected from:
- (a) halo,
- (b) hydroxy,
- 30 (c) -O-C<sub>1</sub>-3alkyl,
- (d) trifluoromethyl, and
- (e) -C<sub>1</sub>-3alkyl,

and where the phenyl and the heterocycle is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- 5 (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- (e) C<sub>1-6</sub>alkyl,
- (f) C<sub>3-7</sub>cycloalkyl,
- 10 (g) -O-C<sub>1-6</sub>alkyl,
- (h) -O-C<sub>3-7</sub>cycloalkyl,
- (i) -SCF<sub>3</sub>,
- (j) -S-C<sub>1-6</sub>alkyl,
- (k) -SO<sub>2</sub>-C<sub>1-6</sub>alkyl,
- 15 (l) phenyl,
- (m) heterocycle,
- (n) -CO<sub>2</sub>R<sup>9</sup>,
- (o) -CN,
- (p) -NR<sup>9</sup>R<sup>10</sup>,
- 20 (q) -NR<sup>9</sup>-SO<sub>2</sub>-R<sup>10</sup>,
- (r) -SO<sub>2</sub>-NR<sup>9</sup>R<sup>10</sup>, and
- (s) -CONR<sup>9</sup>R<sup>10</sup>;

R<sup>3</sup> is -(C<sub>0-6</sub>alkyl)-phenyl,

25 where the alkyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C<sub>1-3</sub>alkyl, and
- 30 (d) trifluoromethyl,

and where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,

- 5
- (c) hydroxy,
  - (d) C<sub>1</sub>-3alkyl,
  - (e) -O-C<sub>1</sub>-3alkyl,
  - (f) -CO<sub>2</sub>R<sup>9</sup>,
  - (g) -CN,
  - (h) -NR<sup>9</sup>R<sup>10</sup>, and
  - (i) -CONR<sup>9</sup>R<sup>10</sup>;

R<sup>4</sup> is selected from:

- 10
- (a) hydrogen,
  - (b) hydroxy,
  - (c) C<sub>1</sub>-6alkyl,
  - (d) C<sub>1</sub>-6alkyl-hydroxy,
  - (e) -O-C<sub>1</sub>-3alkyl,
  - 15 (f) -CO<sub>2</sub>R<sup>9</sup>,
  - (g) -CONR<sup>9</sup>R<sup>10</sup>, and
  - (h) -CN;

or where R<sup>3</sup> and R<sup>4</sup> may be joined together to form a ring which is selected from:

- 20
- (a) 1H-indene,
  - (b) 2,3-dihydro-1H-indene,
  - (c) 2,3-dihydro-benzofuran,
  - (d) 1,3-dihydro-isobenzofuran,
  - (e) 2,3-dihydro-benzothiofuran, and
  - 25 (f) 1,3-dihydro-isobenzothiofuran,

or where R<sup>3</sup> and R<sup>5</sup> or R<sup>4</sup> and R<sup>6</sup> may be joined together to form a ring which is phenyl,

wherein the ring is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- 30
- (a) halo,
  - (b) trifluoromethyl,
  - (c) hydroxy,
  - (d) C<sub>1</sub>-3alkyl,
  - (e) -O-C<sub>1</sub>-3alkyl,
  - 35 (f) -CO<sub>2</sub>R<sup>9</sup>,

- (g) -CN,
- (h) -NR<sup>9</sup>R<sup>10</sup>, and
- (i) -CONR<sup>9</sup>R<sup>10</sup>;

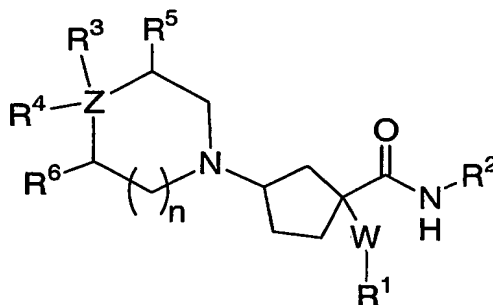
5 R<sup>5</sup> and R<sup>6</sup> are independently selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) C<sub>1</sub>-6alkyl,
- (d) C<sub>1</sub>-6alkyl-hydroxy,
- 10 (e) -O-C<sub>1</sub>-3alkyl,
- (f) oxo, and
- (g) halo;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

15

2. The compound of Claim 1 of the formula Ia:

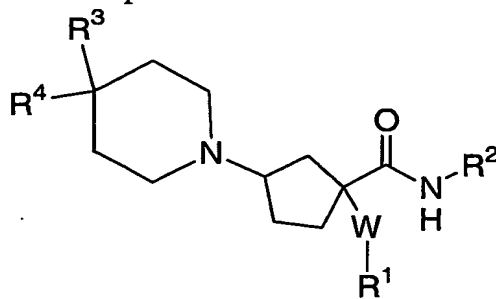


Ia

and pharmaceutically acceptable salts and individual diastereomers thereof.

20

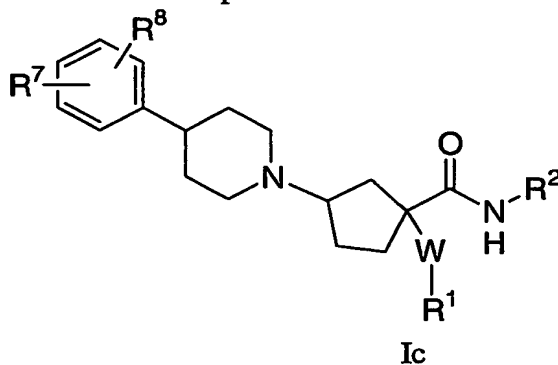
3. The compound of Claim 1 of the formula Ib:



Ib

and pharmaceutically acceptable salts and individual diastereomers thereof.

4. The compound of Claim 1 of the formula Ic:

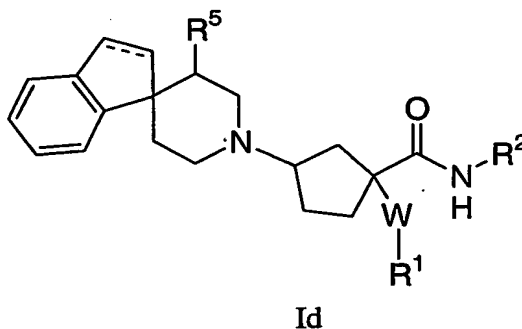


and wherein R<sup>7</sup> and R<sup>8</sup> are independently selected from:

- (a) hydrogen,
- (b) halo,
- (c) trifluoromethyl,
- (d) hydroxy,
- (e) C<sub>1-3</sub>alkyl,
- (f) -O-C<sub>1-3</sub>alkyl,
- (g) -CO<sub>2</sub>H,
- (h) -CO<sub>2</sub>C<sub>1-3</sub>alkyl, and
- (i) -CN;

and pharmaceutically acceptable salts and individual diastereomers thereof.

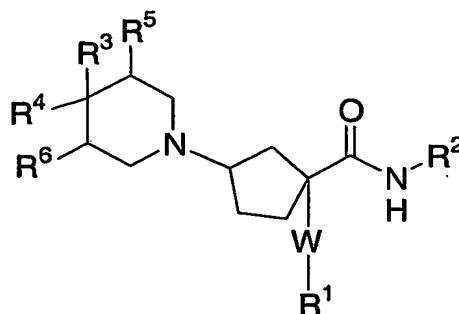
5. The compound of Claim 1 of the formula Id:



wherein the dash line represents either single or double bonds;

and pharmaceutically acceptable salts and individual diastereomers thereof.

6. The compound of Claim 1 of the formula:



5

wherein W is selected from furanyl, imidazolyl, oxadiazolyl, oxazolyl, phenyl, pyrazolyl, pyrazinyl, pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, and thiazolyl, and pharmaceutically acceptable salts and individual diastereomers thereof.

10

7. The compound of Claim 1 wherein W is selected from furanyl, imidazolyl, oxadiazolyl, oxazolyl, phenyl, pyrazolyl, pyrazinyl, pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl, and triazolyl, and N-oxides thereof.

15

8. The compound of Claim 1 wherein X is -CONH-.

9. The compound of Claim 1 wherein Z is -C-, -N- or -O-.

20

10. The compound of Claim 1 wherein n is 0 and 1.

11. The compound of Claim 1 wherein R<sup>1</sup> is selected from:

- (a) hydrogen
- (b) halo
- (c) C<sub>1</sub>-3alkyl,
- (d) -O-C<sub>1</sub>-3alkyl,
- (e) -CO<sub>2</sub>R<sup>9</sup>,
- (f) -S-C<sub>1</sub>-3alkyl,
- (g) -SO<sub>2</sub>-C<sub>1</sub>-3alkyl,

25

- (h) -SCF<sub>3</sub>,
- (i) NHC(=NH)NR<sup>9</sup>R<sup>10</sup>
- (j) -NR<sup>9</sup>R<sup>10</sup>,
- (k) -NR<sup>9</sup>-SO<sub>2</sub>-R<sup>10</sup>,
- (l) -SO<sub>2</sub>-NR<sup>9</sup>R<sup>10</sup>, and
- (m) -CONR<sup>9</sup>R<sup>10</sup>.

12. The compound of Claim 1 wherein R<sup>2</sup> is selected from  
 -(C<sub>0-4</sub>alkyl)-phenyl and -(C<sub>0-4</sub>alkyl)-heterocycle,

where heterocycle is selected from:

furanyl, imidazolyl, oxadiazolyl, oxazolyl, pyrazolyl, pyrazinyl,  
 pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl,  
 and triazolyl, and N-oxides thereof,

where the alkyl is unsubstituted or substituted with 1-7 substituents where the  
 substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C<sub>1-3</sub>alkyl, and
- (d) trifluoromethyl,

and where the phenyl or heterocycle is unsubstituted or substituted with 1-5  
 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- (e) C<sub>1-3</sub>alkyl,
- (f) -O-C<sub>1-3</sub>alkyl,
- (g) -CO<sub>2</sub>R<sup>9</sup>,
- (h) -S-C<sub>1-3</sub>alkyl,
- (i) -SO<sub>2</sub>-C<sub>1-3</sub>alkyl,
- (j) -SCF<sub>3</sub>,
- (k) -CO<sub>2</sub>R<sup>9</sup>,
- (l) -NR<sup>9</sup>R<sup>10</sup>,
- (m) -NR<sup>9</sup>-SO<sub>2</sub>-R<sup>10</sup>,



- (n)  $-\text{SO}_2-\text{NR}^9\text{R}^{10}$ , and
- (o)  $-\text{CONR}^9\text{R}^{10}$ .

13. The compound of Claim 1 wherein  $\text{R}^2$  is selected from  
5  $-(\text{C}_{0-4}\text{alkyl})\text{-phenyl}$  and  $-(\text{C}_{0-4}\text{alkyl})\text{-heterocycle}$ ,  
where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof,  
where the alkyl is unsubstituted or substituted with 1-7 substituents where the  
substituents are independently selected from:

- (a) halo,
- 10 (b) hydroxy,
- (c)  $-\text{O}-\text{C}_{1-3}\text{alkyl}$ , and
- (d) trifluoromethyl,

and where the phenyl or heterocycle is unsubstituted or substituted with 1-3  
substituents where the substituents are independently selected from:

- 15 (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- (e)  $\text{C}_{1-3}\text{alkyl}$ ,
- 20 (f)  $-\text{O}-\text{C}_{1-3}\text{alkyl}$ ,
- (g)  $-\text{CO}_2-\text{C}_{1-3}\text{alkyl}$ ,
- (h)  $-\text{CO}_2\text{H}$ ,
- (i)  $-\text{S}-\text{C}_{1-3}\text{alkyl}$ ,
- (j)  $-\text{SO}_2-\text{C}_{1-3}\text{alkyl}$ ,
- 25 (k)  $-\text{SCF}_3$ ,
- (l)  $-\text{NH}_2$ ,
- (m)  $-\text{NH}-\text{SO}_2-\text{C}_{1-3}\text{alkyl}$ , and
- (n)  $-\text{SO}_2-\text{NH}_2$ .

30 14. The compound of Claim 1 wherein  $\text{R}^2$  is selected from  
 $-\text{CH}_2\text{-phenyl}$  and  $-\text{CH}_2\text{-heterocycle}$ ,  
where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof,  
and where the phenyl or heterocycle is unsubstituted or substituted with 1-3  
substituents where the substituents are independently selected from:

- 5 (a) halo,  
 (b) trifluoromethyl,  
 (c) trifluoromethoxy,  
 (d) hydroxy,  
 (e) C<sub>1-3</sub>alkyl,  
 (f) -O-C<sub>1-3</sub>alkyl,  
 (g) -CO<sub>2</sub>-C<sub>1-3</sub>alkyl,  
 (h) -CO<sub>2</sub>H,  
 (i) -S-C<sub>1-3</sub>alkyl,  
 10 (j) -SO<sub>2</sub>-C<sub>1-3</sub>alkyl,  
 (k) -SCF<sub>3</sub>,  
 (l) -NH<sub>2</sub>,  
 (m) -NH-SO<sub>2</sub>-C<sub>1-3</sub>alkyl, and  
 (n) -SO<sub>2</sub>-NH<sub>2</sub>.

15

15. The compound of Claim 1 wherein R<sup>2</sup> is selected from:

- (1) -CH<sub>2</sub>-(phenyl),  
 (2) -CH<sub>2</sub>-(4-bromophenyl),  
 (3) -CH<sub>2</sub>-(3-chlorophenyl),  
 20 (4) -CH<sub>2</sub>-(3,5-difluorophenyl),  
 (5) -CH<sub>2</sub>-((2-trifluoromethyl)phenyl),  
 (6) -CH<sub>2</sub>-((3-trifluoromethyl)phenyl),  
 (7) -CH<sub>2</sub>-((4-trifluoromethyl)phenyl),  
 (8) -CH<sub>2</sub>-((3-trifluoromethoxy)phenyl),  
 25 (9) -CH<sub>2</sub>-((3-trifluoromethylthio)phenyl),  
 (10) -CH<sub>2</sub>-((3-trifluoromethoxy-5-thiomethyl)phenyl),  
 (11) -CH<sub>2</sub>-((3-trifluoromethoxy-5-methoxy)phenyl),  
 (12) -CH<sub>2</sub>-((3-trifluoromethoxy-5-methanesulfonyl)phenyl),  
 (13) -CH<sub>2</sub>-((3-trifluoromethoxy-5-amino)phenyl),  
 30 (14) -CH<sub>2</sub>-((3-trifluoromethoxy-5-aminomethanesulfonyl)phenyl),  
 (15) -CH<sub>2</sub>-((3-trifluoromethoxy-5-sulfonylamino)phenyl),  
 (16) -CH<sub>2</sub>-((3,5-bis-trifluoromethyl)phenyl),  
 (17) -CH<sub>2</sub>-((3-fluoro-5-trifluoromethyl)phenyl),  
 (18) -CH(CH<sub>3</sub>)-((3,5-bis-trifluoromethyl)phenyl),  
 35 (19) -C(CH<sub>3</sub>)<sub>2</sub>-((3,5-bis-trifluoromethyl)phenyl),

- (20) -CH<sub>2</sub>-(4-(2-trifluoromethyl)pyridyl),  
(21) -CH<sub>2</sub>-(5-(3-trifluoromethyl)pyridyl),  
(22) -CH<sub>2</sub>-(5-(3-trifluoromethyl)pyridazinyl),  
(23) -CH<sub>2</sub>-(4-(2-trifluoromethyl)pyridyl-N-oxide), and  
5 (24) -CH<sub>2</sub>-(5-(3-trifluoromethyl)pyridyl-N-oxide).

16. The compound of Claim 1 wherein R<sup>3</sup> is hydrogen or phenyl, where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- 10 (a) halo,  
(b) trifluoromethyl,  
(c) hydroxy,  
(d) C<sub>1</sub>-3alkyl,  
(e) -O-C<sub>1</sub>-3alkyl,  
15 (f) -CO<sub>2</sub>R<sup>9</sup>,  
(g) -CN,  
(h) -NR<sup>9</sup>R<sup>10</sup>, and  
(i) -CONR<sup>9</sup>R<sup>10</sup>.

20 17. The compound of Claim 1 wherein R<sup>3</sup> is hydrogen or phenyl, where the phenyl is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from:

- (a) halo,  
(c) hydroxy,  
25 (d) C<sub>1</sub>-3alkyl,  
(e) -O-C<sub>1</sub>-3alkyl, and  
(f) -CO<sub>2</sub>R<sup>9</sup>.

18. The compound of Claim 1 wherein R<sup>3</sup> is phenyl,  
30 or para-fluorophenyl.

19. The compound of Claim 1 wherein R<sup>4</sup> is selected from:

- (a) hydrogen,  
(b) hydroxy,

- (c) -CO<sub>2</sub>H,
- (d) -CO<sub>2</sub>C<sub>1-6</sub>alkyl,
- (e) -CN.

5                    20.    The compound of Claim 1 wherein R<sup>5</sup> and R<sup>6</sup> are independently selected from:

- (a)    hydrogen,
- (b)    hydroxy,
- (c)    -CH<sub>3</sub>,
- 10       (d)    -O-CH<sub>3</sub>, and
- (e)    oxo.

                    21.    A compound which is selected from the group consisting of the title compounds of the Examples, and pharmaceutically acceptable salts and  
15    individual diastereomers thereof.

                    22.    A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

20                   23.    A method for modulation of chemokine receptor activity in a mammal in need thereof which comprises the administration of an effective amount of the compound of Claim 1.

                    24.    A method for treating, ameliorating or controlling an  
25    inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

                    25.    A method for reducing the risk of an inflammatory or  
30    immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

26. A method for treating, ameliorating or controlling rheumatoid arthritis which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.